



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/042,059	10/25/2001	Gerd Gellissen	029474-5007	5408

28977 7590 07/27/2004

MORGAN, LEWIS & BOCKIUS LLP
1701 MARKET STREET
PHILADELPHIA, PA 19103-2921

EXAMINER

LAMBERTSON, DAVID A

ART UNIT	PAPER NUMBER
----------	--------------

1636

DATE MAILED: 07/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/042,059

Applicant(s)

GELLISSEN ET AL.

Examiner

David A. Lambertson

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 August 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-33 is/are pending in the application.
- 4a) Of the above claim(s) 20-33 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-18 is/are rejected.
- 7) ☒ Claim(s) 19 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign-priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. 10/042,059.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

This Office Action is sent in response to the Petition to Withdraw Holding of Abandonment, filed August 1, 2003 and approved on February 6, 2004. The Office Action constitutes a Non-final Office Action because the initial Non-final Office Action was not received by Applicant.

Election/Restrictions

Applicant's election without traverse of Group I (claims 1-19) in Paper No. 9 is acknowledged.

Claims 20-33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 9.

Claims 1-19 are ready for examination in the pending application.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Art Unit: 1636

Priority

Applicant is advised of possible benefits under 35 U.S.C. 119(a)-(d), wherein an application for patent filed in the United States may be entitled to the benefit of the filing date of a prior application filed in a foreign country.

Acknowledgment is made of applicant's claim for priority based on an application filed in Europe on April 27, 2000. It is noted, however, that applicant has not filed a certified copy of the PCT, or an English translation of the PCT (which was not published in English).

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Germany on April 27, 1999. It is noted, however, that applicant has not filed a certified copy of the foreign application as required by 35 U.S.C. 119(b), or an English translation thereof.

Specification

The disclosure is objected to because of the following informalities: on page 14 line 8, it appears that applicant has misrepresented a 3.2 kb BglIII fragment as being 3.2 kilograms; on line 10 of the same page, it appears applicant has misrepresented a 3.0 kb BglIII fragment as being 3.0 base pairs.

Appropriate correction is required.

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: the claims contain the negative limitation "that the nucleic acid molecule does not include the nucleic acid sequence of the *ARO7* gene from *Saccharomyces cerevisiae*."

Art Unit: 1636

The specification, while mentioning the *ARO7* gene on page 4, does not indicate support for the negative limitation recited in the claims. Applicant must amend the specification to contain antecedent basis for the limitation.

The disclosure is objected to because of the following informalities: the specification does not contain section headings. The specification does not contain an indication of where the BACKGROUND OF THE INVENTION, SUMMARY OF THE INVENTION or DETAILED DESCRIPTION OF THE INVENTION begins/ends. Of a particularly important note, the specification does not make note as to where the BRIEF DESCRIPTION OF THE DRAWINGS begins, although it appears to begin on page 17 of the specification. Applicant is required to indicate the appropriate section headings as set forth in 37 CFR 1.77(b).

Claim Objections

Claim 19 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to claims in the alternative only. See MPEP § 608.01(n). Accordingly, the claim has not been further treated on the merits.

Claims 1-18 are objected to because of the following informalities: all claims should begin with an article. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-9 and 12-18 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. In this instance, applicant is claiming a nucleic acid, host cells containing the nucleic acid and a process for producing a polypeptide using the nucleic acid. This subject matter is non-statutory because the hand of man is not obvious in the inventive process of the nucleic acid, recited in claim 1. All of the indicated claims depend from claim 1 without any additional limitations to show the involvement of the "hand of man", therefore all of the claims are non-statutory. Indication that the nucleic acid is isolated would be remedial. Claims 10 and 11 indicate additional limitations which include heterologous sequences, thus indicate the involvement of the "hand of man".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims fragments and variants of a nucleic acid encoding for a protein having chorismate mutase activity, wherein the nucleic acid sequence is initially represented by SEQ ID NO: 1. The variants set forth in the claims can include additions, deletions, insertions and inversions, and include nucleic acids with as little as 60% homology. The claims read on a broad

Art Unit: 1636

genus of fragments and variants of SEQ ID NO: 1 that must necessarily encode a protein having chorismate mutase activity. It is especially noted that in section (h) of claim 1, the claim reads on a fragment of a nucleic acid with 60% homology, and therefore can read on a fragment having no sequence identity to SEQ ID NO: (e.g., if the entire 5' end of the DNA is the 40% having no identity to SEQ ID NO: 1, this fragment having no identity to SEQ ID NO: 1 can be chosen). Thus, the skilled artisan must also be able to envision nucleic acid fragments without any homology to SEQ ID NO: 1 that have chorismate mutase activity.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicants were in possession of the claimed genus. In the instant case, the specification does not sufficiently describe a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics.

Applicant claims a fragment or variant (including those having as little as 60% homology) of SEQ ID NO: 1 that must encode a protein having chorismate mutase activity by function only, without any disclosed or known correlation between the elements and their function. The specification only provides teachings regarding SEQ ID NO: 1 and its ability to encode a protein having chorismate mutase activity. The specification does not teach how to envision a fragment having as little as 60% homology with SEQ ID NO: 1 that necessarily has chorismate mutase activity because there is no indication of a structure-function relationship for

Art Unit: 1636

the protein encoded by SEQ ID NO: 1 and the required activity, and there is a lack of representative examples to define the claimed genus. There is no indication in the specification as to what 40% of the molecule can be deleted or mutated while still maintaining the activity; i.e., what domains are required to maintain the structural properties of the enzyme such that it maintains chorismate activity. Without such information, the skilled artisan cannot envision which additions, deletions, insertions or inversions of SEQ ID NO: 1 would necessarily encode a protein having chorismate mutase activity. Furthermore, the skilled artisan would be unable to envision fragments that have no relationship to SEQ ID NO: 1, yet retain chorismate mutase activity; this is based upon a claim to fragments of nucleic acids having only 60% homology to SEQ ID NO: 1. Since the skilled artisan cannot envision a sufficient number of embodiments of the instant invention from the instant specification, the claims lack written description.

The prior art does not provide sufficient information on the subject to overcome the deficiencies of the instant specification. There is no description in the prior art that allows one to envision a representative number of fragments or variants (including those having as little as 60% homology) of SEQ ID NO: 1 that must encode a protein having chorismate mutase activity by disclosing structural or functional features of the protein encoded by SEQ ID NO: 1. The claims are predicated on a presumption of conservation of activity that depends solely on the degree of homology between nucleic acids (which translates into a degree of homology between the encoded proteins). However, the prediction of function based on sequence homology is an unpredictable art. This was demonstrated by the conflicting publications of Scott *et al.* (*Nature Genetics* 21: 440-443, 1999; see entire document; henceforth Scott) and Everett *et al.* (*Nature Genetics* 17: 411-422, 1997; see entire document; henceforth Everett) regarding the cloning and

Art Unit: 1636

characterization of PDS. Everett initially identified and sequenced the protein, predicting based upon the sequence that the PDS gene product functioned as a sulphate ion transporter protein because of its similarity to a family of known sulphate ion transporters (see for example the Abstract and page 419, right column, second full paragraph). However, further characterization done by Scott indicated that PDS was not a sulphate ion transporter because it was unable to transport sulphate ions; rather, Scott identified that PDS was a chloride and iodide ion transporter (see for example the Abstract and page 440, the paragraph bridging the left and right columns to the second full paragraph). Scott further indicated that their results underscored the importance of establishing function even in the face of significant homology to proteins of known function (see for example page 441, left column, third full paragraph), thereby establishing that function based on homology is an unpredictable endeavor. Thus the skilled artisan cannot rely on the prior art to envision a sufficient number of embodiments of the instant invention, based on sequence homology alone, to see that the applicant was in possession of the claimed genus.

Neither the specification of the instant application or the prior art teaches a structure-function relationship for a representative number of nucleic acids having 60% homology to SEQ ID NO: 1, or fragments or variants thereof, which necessarily encode a protein with chorismate mutase activity. As a result, the skilled artisan would not be able to envision the claimed invention by relying on the teachings of the prior art or the instant specification. Therefore applicant has not satisfied the written description requirement to show the skilled artisan that they were in possession of the claimed genus.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

Art Unit: 1636

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (and all dependent claims) is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. The claim states "a nucleic acid *with* the DNA sequence..." in part (a) of the claim. It is unclear if "with" represents open or closed language, making it impossible to appropriately analyze the claim.

Claim 1 (and all dependent claims) is further rejected under 35 U.S.C. 112, second paragraph, because it is unclear what is meant by the limitation "a combination of several of the nucleic acids stated in (a) to (g)." For example, it is unclear if gene fusions are being claimed (i.e., a covalent combination of several nucleic acids from (a) to (f)), or if a collective pool of the nucleotides are being claimed (e.g., a library of nucleic acids).

Claim 11 is rejected under 35 U.S.C. 112, second paragraph, because it is unclear what applicant means by "a heterologous nucleic acid sequence suitable for expression and optionally secretion." For example, it is unclear if the claim referring to a heterologous sequence encoding a distinct protein that can be suitably expressed along with the nucleic acid represented by SEQ ID NO: 1, or if the claim is reciting a limitation for including a heterologous promoter or signal (secretion) sequence that is suitable for use with the nucleic acid of SEQ ID NO: 1.

The term "suitable for expression" in claims 9, 11, 14 and 17 is a relative term which renders the claim indefinite. The term "suitable for expression" is not defined by the claim, the

Art Unit: 1636

specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear what would be “suitable for expression”, either in terms of a promoter sequence or a host cell, or as it pertains to claim 11, any heterologous sequence. For example, it is unclear if there are sequences that would be “unsuitable” for expression of this particular sequence.

Claims 14 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. It is unclear how the skilled artisan would discern if a cell were naturally occurring versus non-naturally occurring. The term “recombinant” would be remedial.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by “such as” and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 16 recites the broad recitation “mammalian cells,” and the claim also recites “CHO cells, COS cells and HeLa cells” which is the narrower statement of the range/limitation. Additionally, claim 16 recites the broad limitation yeast cells,

Art Unit: 1636

followed by the more narrow limitation “such as *Hansenula polymorpha* and *Saccharomyces cerevisiae*.”

Regarding claim 16, the phrase “such as” renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claims 15 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. The claims appear to recite Markush groups, but do not use the appropriate language format by stating “the group consisting of” prior to listing the members. Additionally, in claim 16, applicant uses multiple conjunctions that confuse what the members are actually in the group(s). Use of a single conjunction following the penultimate member of the group will be remedial.

Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. It is unclear what the term “naturally modified” is intended to indicate. Does the limitation mean any modification that occurs in nature, or does the limitation specify any modification that happens to the enzyme in its natural state/environment?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Art Unit: 1636

Claim 1 reads on a specific chorismate mutase, but contains limitations that include “variants”(1(f)) and “fragments” (1(g)) of the enzyme, as well as variants and fragments of a nucleic acid having as little as 60% homology to SEQ ID NO: 1. Thus the sequence as claimed reads on nucleic acids with little or no sequence homology to SEQ ID NO: 1, so long as said sequence encodes a protein having chorismate mutase activity. As such, the claims read on any chorismate mutase from any organism, which serves as a basis for the following rejections.

Claims 1, 2, 7-9, 11, 12, 14, 15, 17 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Gray *et al.* (*Biochem.* **29**(2): 376-383, 1990; see entire document).

Gray *et al.* teach the molecular cloning of a chorismate mutase gene (DNA) from *Bacillus subtilis* (*aroH*) into both a phagemid vector and a pUC13 vector, where the gene is “positioned behind efficient transcription and translation” sequences (e.g., a promoter sequence “suitable” for expression); since these sequences are not native to the *Bacillus subtilis aroH*, they represent heterologous sequences “suitable for expression”, as per claims 9 and 11 (see for example, the Abstract and page 377, right side, last paragraph continuing to page 378). Gray *et al.* also teach transforming this construct into *E. coli* where the nucleic acid/resulting polypeptide is produced, evidenced by the purification of the enzyme (see for example Tables I and II).

Furthermore, since the enzyme that was purified from the aforementioned *E. coli* cells was functional (see for example Tables I and II), and absent evidence to the contrary, the produced polypeptide must necessarily contain any “naturally occurring” modifications. Gray *et al.* further characterize the specific activity of the purified chorismate mutase as $200 \mu\text{mol min}^{-1} \text{mg}^{-1}$ (see Tables I and II). However, since Gray *et al.* make use of alternative enzymatic assay conditions

Art Unit: 1636

compared to those used in the instant application, it is impossible to make a direct comparison of the specific activities of the two chorismate mutases. In view of the catalytic data provided by Gray *et al.* and absent evidence to the contrary, an inherent property of the enzyme that “necessarily flows” from the teachings of the prior art is that it has at least 10%, 50% and 75% chorismate mutase activity.

Because the Office does not have the facilities for examining and comparing the applicant’s product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See *in re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claim 1, 2, 7-9, 11, 12, 14, 15, 17 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Eberhard *et al.* (*The Plant J.* 10(5): 815-821, 1996; see entire document).

Eberhard *et al.* describe the cloning of an *A. thaliana* chorismate mutase gene (DNA) by complementation of a chorismate mutase deficient *E. coli* strain (see for example page 815, right side, last paragraph). The gene was cloned into expression vector pTrc99A, whereby the gene was operably linked to an efficient promoter (transcription) sequence “suitable for expression” as evidenced by the ability of the gene to complement the *E. coli* strain (see for example page 818, first full paragraph and page 820, left side, the penultimate paragraph); since these sequences are not native to the *A. thaliana* chorismate mutase gene, they represent heterologous sequences “suitable for expression”, as per claims 9 and 11. Eberhard *et al.* also teach transforming this

Art Unit: 1636

construct into *E. coli* where the nucleic acid/resulting polypeptide is produced, evidenced by the purification of the enzyme (see for example page 818, first full paragraph and Table 1).

Furthermore, since the enzyme that was purified from the aforementioned *E. coli* cells was functional, and absent evidence to the contrary, the produced polypeptide must necessarily contain "naturally occurring" modifications. Since the gene was initially identified via complementation of a mutation in a known chorismate mutase, the enzyme must inherently have the catalytic activity of a chorismate mutase. Therefore, it is an inherent property of the enzyme that it has at least 10%, 50% and 75% chorismate mutase activity because, when considering the complementation data, the property of having at least 10%, 50% and 75% chorismate mutase activity "necessarily flows" from the teachings of the prior art. Eberhard *et al.* further characterize the specific activity of the purified chorismate mutase as $1290 \text{ nmol min}^{-1} \text{ mg}^{-1}$ (see Table 1), although they make use of alternative enzymatic assay conditions than those used in the instant application (see for example page 820, left side, last paragraph).

Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See *in re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Applicant is advised that a number of additional chorismate mutases from different organisms are known in the art (see Figure 1 of MacBeath *et al.*, *Biochemistry* **37**: 10062-10073,

Art Unit: 1636

1998, for a brief listing of related chorismate mutases). Many of these enzymes read on the limitation of at least claim 1 for the reasons set forth above considering the limitations of claim 1(f) and 1(g). In the interest of limiting the size of the Office Action, not all of these enzymes are presented as prior art rejections. However, it is expected that applicant is now aware that additional art rejections not present in the Office Action also apply to the claims in their current embodiment.

Allowable Subject Matter


No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A Lambertson whose telephone number is (703) 308-8365. The examiner can normally be reached on 8am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to receptionist whose telephone number is (703) 308-0196.

David A. Lambertson
July 9, 2004


JAMES KETTER
PRIMARY EXAMINER